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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/565,126

09/18/2006

Guido Grandi

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EXAMINER

BASKAR, PADMAVATHI

ART UNIT

PAPER NUMBER

1645

MAIL DATE

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05/08/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/565,126	Applicant(s) GRANDI ET AL.	
	Examiner Padma V. Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-10,14,21,23,28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-10,14,23,28 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/19/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's response to restriction filed on 9/22/08 is acknowledged and entered.

Election

2. Applicant's election of Group I (claims 1-14 and 23) and the combination of Spy 0269 (GAS 40, SEQ ID NO:1) and Spy0416 (GAS 57, SEQ ID NO:115) is acknowledged. Applicants also elect SEQ ID NO:1 with traverse. The traversal is on the ground(s) that entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. This is not found persuasive because MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required. The term "distinct" is defined to "mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.01). In the instant situation, the inventions of the Groups are drawn to distinct inventions which are related as separate products capable of separate manufacture, use or sale as described in the previous Office Action. In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. In the instant case a burden has been established in showing that the inventions of the Groups are classified separately necessitating different searches of issued U.S. Patents. However, classification of subject matter is merely one indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive clearly different searches and issues are involved in the examination of each Group.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

3. Claims 3, 11-13, 15-20, 22 and 24-27 are canceled.
Claims 1, 4-5, 10 and 14 have been amended.
New claims 28 and 29 have been added.
Claims 1-2, 4-10, 14, 21, 23, and 28-29 are pending.
Claims 1-2, 4-10, 14, 23, and 28-29 are under examination. Applicant elected Spy 0269 (SEQ ID NO:1). However, applicant did not inform the examiner SEQ ID NO for Spy0416.

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Claim 21 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group of inventions

Associate Power Of Attorney

4. Applicant filed 9/23/08 an associate power of attorney to recognize all attorneys and representatives associated with Customer Number 27476 to prosecute this patent application. These papers are not processed because the office no longer considers associate power of attorney with different customer number. If applicant wants to include other attorneys, then applicant should include them in the same Customer Number i.e., 22907.

Specification Objection

5. It is noted that sequence identification numbers present in the specification are not consistent with the sequence listing submitted on 1/19/06 as compact disc and the paper copy of said sequence listing.

For example: SEQ.ID.NO:2 in the specification is a DNA sequence whereas in the sequence listing it is an amino acid sequence.

SEQ.ID.NO:116 in the specification is an amino acid sequence whereas in the sequence listing it is a DNA sequence.

SEQ.ID.NO:3 in the specification is an amino acid sequence whereas in the sequence listing it is a DNA sequence.

SEQ.ID.NO: 66 in the specification is a DNA sequence whereas in the sequence listing it is an amino acid sequence.

Further applicant submitted SEQ.ID.NOS 1-136 in the sequence listing. However, SEQ.ID.NOS 134 and 135 are missing in the specification.

Sequence Requirements

6. In order to have compact prosecution a first office action can be performed on this application, however, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. The disclosure contains sequences that need SEQ ID numbers on page 45 (gex NN linker and gex NNH linker and page 46(oligos)). Applicant is reminded to check the entire disclosure to ensure that the application is in sequence compliance.

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Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1,2 4-10 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 are vague and indefinite in the recitation of antibodies "Spy 0269" and "Spy0416" as the sole means of identifying the antigen. The use of laboratory designations to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct antigen. For example, "Spy 0269" is also known in the art as Lactobacillus putative surface exclusion protein (Journal of Dairy Science, , 92:870-886, 2009). As such, the skilled artisan would not know the metes and bounds of the recited antigens. This rejection can be overcome by amending the claims to specifically and uniquely identify antigens "Spy 0269" and "Spy0416", for example, by SEQ ID numbers.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-2, 4-10, 14, and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Biswas et al Infection and Immunity, November 2001, Vol. 69, No. 11, p. 7029-7038.

Claims are drawn to an immunogenic composition comprising a combination of *Streptococcus pyogenes* (GAS) antigens, said combination consisting of two to ten GAS antigens, wherein said combination includes a Spy0269 antigen wherein said combination of GAS antigens further includes a Spy0416 antigen, wherein said Spy0269 antigen comprises an amino acid sequence comprising a first coiled-coil region and a second coiled-coil region, wherein the Spy0269 antigen comprises an amino acid sequence comprising a first coiled-coil region, wherein said first coiled-

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coil region comprises an amino acid sequence comprising SEQ ID NO: 12, wherein the Spy0269 antigen comprises an amino acid sequence comprising a second coiled-coil region, wherein said second coiled-coil region includes a leucine zipper region, wherein the second coiled-coil region comprises an amino acid sequence comprising SEQ ID NO: 13, wherein the Spy0269 antigen comprises SEQ ID NO: 1.

Claim 10 is drawn to an immunogenic composition comprising a Spy0269 antigen and a Spy0416 antigen, wherein said Spy0269 antigen is selected from an amino acid sequence comprising (a) a first coiled-coil region, (b) a second coiled-coil region or (c) a first coiled-coil region and a second coiled-coil region, wherein the Spy0269 antigen comprises SEQ ID NO:1

Biswas et al disclose a composition comprising whole cell wall preparation that contains protein antigens from Group A Streptococcus pyogenes (GAS) (see page 7030, right column, third paragraph, said disclosed proteins (i.e., combination of 2-10 antigens) are reacted to Monoclonal antibodies (figure 6). As the composition comprising proteins are reacted to antibodies, the composition is an immunogenic composition. In the absence of evidence to the contrary the combination of these proteins include Spy0269 and Spy0416. Further the art teaches that M proteins have a dimeric alpha-helical coiled structure including first coiled-coil region and a second coiled-coil region that includes leucine zipper region in the hydrophobic region (see page 7029, right column, first paragraph). Although the prior art does not teach SEQ.ID.NO:1, 12 and 13 given that the proteins come from the same source S.pyogenes as instantly claimed and having dimeric alpha-helical coiled structure including first coiled-coil region and a second coiled-coil region it is inherent that this composition comprises reads on the claimed invention. Characteristics such as SEQ.ID.NO:1, 12 and 13 are considered inherent characteristics of said protein Spy0269. Since the Office does not have the facilities for examining and comparing applicants immunogenic composition with the prior art immunogenic composition the burden is on applicant to show a novel or unobvious difference between the claimed immunogenic composition and the immunogenic composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. The prior art anticipated the claimed invention.

11. Claims 1-2, 4-10, 14, and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Telford J et al WO200234771-A2 (Publication date 02-MAY-2002). The document is not attached to this action as it is over 4000 pages.

Claims have been discussed supra.

Telford J et al disclose S.pyogenes protein antigens SEQ ID NO 9188 (Spy 0269 page 4042), SEQ ID NO 6298 (Spy0416, page 3795), GAS 127 (example 2388) and 128 (example 2389) etc. The prior art discloses pharmaceutical composition (i.e., immunogenic composition) comprising said

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polypeptides (see abstract and pages 19-20) can be used for vaccine purposes. Thus it read on claims 1, 2, 10, 28-29 because it contains combination of 2 antigens. SEQ ID NO 9188 is 100% identical to Spy 0269 (SEQ.ID.NO:1) and SEQ ID NO 6298 is 99.9% identical to Spy 0461. As the art teaches that M proteins have a dimeric alpha-helical coiled structure including first coiled-coil region and a second coiled-coil region that includes leucine zipper region in the hydrophobic region (see Biswas et al above), the disclosed protein SEQ ID NO 9188 which is 100% identical to Spy 0269 comprises a first coiled-coil region, a second coiled-coil region or a first coiled-coil region(SEQ.ID.NO:12) and a second coiled-coil region (SEQ.ID.NO:13) and thus read on claims 4-9, 14. The prior art anticipated the claimed invention.

PN WO200234771-A2.
 XX
 PD 02-MAY-2002.
 XX
 PF 29-OCT-2001; 2001WO-GB004789.
 XX
 PR 27-OCT-2000; 2000GB-00026333.
 PR 24-NOV-2000; 2000GB-00028727.
 PR 07-MAR-2001; 2001GB-00005640.
 XX
 PA (CHIR) CHIRON SPA.
 PA (GENO-) INST GENOMIC RES.
 XX
 PI Telford J, Massignani V, Margarit Y RosI, Grandi G, Fraser C;
 PI Tettelin H;
 PS Claim 1; Page 4042; 4525pp; English.

Streptococcus polypeptide SEQ ID NO 9188.

Query Match 100.0%; Score 4309; DB 1; Length 873;
 Best Local Similarity 100.0%; Pred. No. 5.3e-267;
 Matches 873; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MDLEQTKPNQVQKQIALTSTIALLSASVGVSHQVKADDRASGETKASNTHDDSLPKPETI	60
Db	1	MDLEQTKPNQVQKQIALTSTIALLSASVGVSHQVKADDRASGETKASNTHDDSLPKPETI	60
Qy	61	QEAKATIDAVEKTL SQKAE LTELATALT KTTAE INHLKEQQDNEQKAL TSAQE IYTNTL	120
Db	61	QEAKATIDAVEKTL SQKAE LTELATALT KTTAE INHLKEQQDNEQKAL TSAQE IYTNTL	120
Qy	121	ASSEETLLAQGAEHQRELTATETELHNAQADQHSKETALSEQKASISAE TTRAQDLVEQV	180
Db	121	ASSEETLLAQGAEHQRELTATETELHNAQADQHSKETALSEQKASISAE TTRAQDLVEQV	180
Qy	181	KTSEQNIAKLNAMISNPDAITKAAQTANDNTKALSSELEKAKADLENQKAKVKKQLTEEL	240
Db	181	KTSEQNIAKLNAMISNPDAITKAAQTANDNTKALSSELEKAKADLENQKAKVKKQLTEEL	240
Qy	241	AAQKAALAEKEAELSRKSSAPSTQDSIVGNNTMKAPQGYPLEELKKLEASGYIGSASYN	300
Db	241	AAQKAALAEKEAELSRKSSAPSTQDSIVGNNTMKAPQGYPLEELKKLEASGYIGSASYN	300
Qy	301	NYEKEHADQIIAKASPGNQLNQYQDIPADRNRFDVDPDLTPEVQNELAQFAAHMINSVRR	360
Db	301	NYEKEHADQIIAKASPGNQLNQYQDIPADRNRFDVDPDLTPEVQNELAQFAAHMINSVRR	360
Qy	361	QLGLPPVTVTAGSQEFARLLSTSYKKTGHGNTSRPSFVYGQPGVSGHYGVGPHDKTIIEDSA	420

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Db      361  QLGLPPVTVTAGSQEFARLLSTSYKKTHGNTRPSFVYGQPGVSGHYGVGPHDKTIIEDSA  420
Qy      421  GASGLIRNDDNMYENIGAFNDVHTVNGIKRGIYDSIKYMLFTDHLHGNTYGHAINFLRVD  480
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421  GASGLIRNDDNMYENIGAFNDVHTVNGIKRGIYDSIKYMLFTDHLHGNTYGHAINFLRVD  480
Qy      481  KHNPNAPVYLGFSSTNVGSLNEHFVMFPESNIANHQRFNKTPIKAVGSTKDYAQRVGTVS  540
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481  KHNPNAPVYLGFSSTNVGSLNEHFVMFPESNIANHQRFNKTPIKAVGSTKDYAQRVGTVS  540
Qy      541  DTIAAIKGVSSLENRLSAIHQEADIMAAQAKVSQQLQGKLASTLKQSDSLNLQVRQLNDT  600
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541  DTIAAIKGVSSLENRLSAIHQEADIMAAQAKVSQQLQGKLASTLKQSDSLNLQVRQLNDT  600
Qy      601  KGSRLTELLAAKAKQAQLEATRDQSLAKLASLKAALHQTEALAEQAAARVTALVAKKAHL  660
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      601  KGSRLTELLAAKAKQAQLEATRDQSLAKLASLKAALHQTEALAEQAAARVTALVAKKAHL  660
Qy      661  QYLKDFKLPNPNRLQVIRERIDNTKQDLAKTTSSLLNAQEALALQAKQSLEATIATTEH  720
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      661  QYLKDFKLPNPNRLQVIRERIDNTKQDLAKTTSSLLNAQEALALQAKQSLEATIATTEH  720
Qy      721  QLTLLKTLANEKEYRHLDEDIATVPDLQVAPPLTGKPLSYSKIDTTPLVQEMVKETKQL  780
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      721  QLTLLKTLANEKEYRHLDEDIATVPDLQVAPPLTGKPLSYSKIDTTPLVQEMVKETKQL  780
Qy      781  LEASARLAAENTSLVAEALVGQTSEMVASNAIVSKITSSITQPSSKTSYSGSGSSTSNLI  840
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      781  LEASARLAAENTSLVAEALVGQTSEMVASNAIVSKITSSITQPSSKTSYSGSGSSTSNLI  840
Qy      841  SDVDESTQRALKAGVVMLAAVGLTGFRFRKESK  873
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      841  SDVDESTQRALKAGVVMLAAVGLTGFRFRKESK  873

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Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biswas et al or Telford J et al.

Claim 23 is drawn to a kit comprising an immunogenic composition comprising a combination of *Streptococcus pyogenes* (GAS) antigens, said combination consisting of two to ten GAS antigens, wherein said combination includes a Spy0269 antigen.

Immunogenic composition have been discussed and rejected above in Biswas et al or Telford J et al. However, the prior art does not teach a kit comprising said immunogenic composition.

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed in the form of a kit with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention and furthermore the claim would have been obvious because the kit is well known in the art and within the capabilities of one skilled in the art. Also of important note is the fact that a person of ordinary skill in the art has good reason to pursue the known option of keeping the antigens in a kit format for the convenience and economy of the user which is within his or her technical grasp and therefore it is not the product of innovation but of ordinary skill and common sense.

16. Claim 1-2, 4-10, 14, and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dale 1999 New vaccines and new vaccine technology, 13:227-243 in view of Ferretti et al PNAS 2001, 98:4658-4663.

Dale discloses an multivalent vaccine (immunogenic composition comprising combination of antigens) comprising M proteins extracted from streptococci mixed together comprising a combination of 8 GAS antigens (see page 230, fourth paragraph first four lines, figure 2 and page 233, first paragraph, first 8 lines) and the combination included M1 protein. Dale in particular does not teach composition comprising g Spy0269 antigen and Spy0416 antigen. However, Ferretti et al discloses 40 virulent associated proteins (see Table 1), out of which thirteen predicted surface proteins containing LPXTG

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motif such as M protein(see page 4661, right column, second paragraph, first two lines) including Accession number Q9A1H3 and Q9A180 that are 100% identical to SEQ.ID.NO:1 and Spy0416 as shown below. Q9A1H3 comprises first coiled antigen and second coiled antigen and a leucine zipper as the disclosed antigen is 100% identical to Spy0269. The art suggests that this new putative virulence proteins would allow towards answering questions related to pathogenesis of streptococcal disease that ultimately lead to improved prevention/treatment (see page 4662, right column, last paragraph).

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Q9A1H3_STRP1
ID   Q9A1H3_STRP1                Unreviewed;          873 AA.
AC   Q9A1H3; Q490X0;
DT   01-JUN-2001, integrated into UniProtKB/TrEMBL.
DT   01-JUN-2001, sequence version 1.
DT   24-JUL-2007, entry version 22.
DE   Putative surface exclusion protein.
GN   Name=prgA; OrderedLocusNames=M5005_Spy0229, SPy_0269;
OS   Streptococcus pyogenes serotype M1.
OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
OC   Streptococcus.
OX   NCBI_TaxID=301447;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RC   STRAIN=ATCC 700294 / SF370 / Serotype M1;
RX   MEDLINE=21192684; PubMed=11296296; DOI=10.1073/pnas.071559398;
RA   Ferretti J.J., McShan W.M., Ajdic D.J., Savic D.J., Savic G., Lyon K.,
RA   Primeaux C., Sezate S., Suvorov A.N., Kenton S., Lai H.S., Lin S.P.,
RA   Qian Y., Jia H.G., Najjar F.Z., Ren Q., Zhu H., Song L., White J.,
RA   Yuan X., Clifton S.W., Roe B.A., McLaughlin R.E.;
RT   "Complete genome sequence of an M1 strain of Streptococcus pyogenes.";
RL   Proc. Natl. Acad. Sci. U.S.A. 98:4658-4663(2001).
RN   [2]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RC   STRAIN=ATCC BAA-947 / MGAS5005 / Serotype M1;
RX   PubMed=16088826; DOI=10.1086/432514;
RA   Sumby P., Porcella S.F., Madrigal A.G., Barbian K.D., Virtaneva K.,
RA   Ricklefs S.M., Sturdevant D.E., Graham M.R., Vuopio-Varkila J.,
RA   Hoe N.P., Musser J.M.;
RT   "Evolutionary origin and emergence of a highly successful clone of
RT   serotype M1 group A Streptococcus involved multiple horizontal gene
RT   transfer events.";
RL   J. Infect. Dis. 192:771-782(2005).
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CC   -----
DR   EMBL; AE004092; AAK33344.1; -; Genomic_DNA.
DR   EMBL; CP000017; AAZ50848.1; -; Genomic_DNA.
DR   GenomeReviews; AE004092_GR; M5005_Spy0229.
DR   GenomeReviews; CP000017_GR; prgA.
DR   BioCyc; SPY0160490:SPY0269-MONOMER; -.
PE   4: Predicted;
KW   Complete proteome.
SQ   SEQUENCE   873 AA;   94697 MW;   0CF6454F539366E0 CRC64;

Query Match          100.0%; Score 4309; DB 2; Length 873;
Best Local Similarity 100.0%; Pred. No. 1.1e-167;
Matches 873; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy      1 MDLEQTKPNQVKQKIALTSTIALLSASVGVSHQVKADDRASGETKASNTHDDSLPKPETI 60
        |
Db      1 MDLEQTKPNQVKQKIALTSTIALLSASVGVSHQVKADDRASGETKASNTHDDSLPKPETI 60

Qy      61 QEAKATIDAVEKTLSSQKAELELATALTKTTAEINHLKEQQDNEQKALTSQAQEIYNTNL 120
        |

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Db	61	QEAKAIDAVEKTLSSQKAELETALATLTKTTAEINHLKEQQDNEQKALTSAQEIYNTNL	120
Qy	121	ASSEETLLAQGAEHQRELATATETELHNAQADQHSKETALSEQKASISAETTRAQDLVEQV	180
Db	121	ASSEETLLAQGAEHQRELATATETELHNAQADQHSKETALSEQKASISAETTRAQDLVEQV	180
Qy	181	KTSEQNIAKLNAMISNPDAITKAAQTANDNTKALSSELEKAKADLENQKAKVKKQLTEEL	240
Db	181	KTSEQNIAKLNAMISNPDAITKAAQTANDNTKALSSELEKAKADLENQKAKVKKQLTEEL	240
Qy	241	AAQKAALAEKEAELSRLKSSAPSTQDSIVGNNTMKAPQGYPLEELKKLEASGYIGSASYN	300
Db	241	AAQKAALAEKEAELSRLKSSAPSTQDSIVGNNTMKAPQGYPLEELKKLEASGYIGSASYN	300
Qy	301	NYKKEHADQIIAKASPGNQLNQYQDIPADRNRFPDPDLNLTPEVQNELAQFAAHMINSVRR	360
Db	301	NYKKEHADQIIAKASPGNQLNQYQDIPADRNRFPDPDLNLTPEVQNELAQFAAHMINSVRR	360
Qy	361	QLGLPPVTVTAGSQEFARLLSTSYYKTHGNTRPSFVYGQPGVSGHYGVGPHDKTIIEDSA	420
Db	361	QLGLPPVTVTAGSQEFARLLSTSYYKTHGNTRPSFVYGQPGVSGHYGVGPHDKTIIEDSA	420
Qy	421	GASGLIRNDDNMYENIGAFNDVHTVNGIKRGIYDSIKYMLFTDHLHGNTYGHAINFLRVD	480
Db	421	GASGLIRNDDNMYENIGAFNDVHTVNGIKRGIYDSIKYMLFTDHLHGNTYGHAINFLRVD	480
Qy	481	KHNP NAPVYLGFSTSNVGSLSNEHFVMFPESNIAHQRFNKTPIKAVGSTKDYAQRVGTVS	540
Db	481	KHNP NAPVYLGFSTSNVGSLSNEHFVMFPESNIAHQRFNKTPIKAVGSTKDYAQRVGTVS	540
Qy	541	DTIAAIAIKGVSSLENRLSAIHQEADIMAAQAKVSQLQGKLASTLTKQSDSLNLQVRQLNDT	600
Db	541	DTIAAIAIKGVSSLENRLSAIHQEADIMAAQAKVSQLQGKLASTLTKQSDSLNLQVRQLNDT	600
Qy	601	KGSLRTELLEAAKAKQAQLEATRDQSLAKLASLKAALHQTEALAEQAAARVTALVAKKAHL	660
Db	601	KGSLRTELLEAAKAKQAQLEATRDQSLAKLASLKAALHQTEALAEQAAARVTALVAKKAHL	660
Qy	661	QYLRDFKLNPNRLQVIRERIDNTKQDLAKTTSSLLNAQEALAAALQAKQSSLEATIATTEH	720
Db	661	QYLRDFKLNPNRLQVIRERIDNTKQDLAKTTSSLLNAQEALAAALQAKQSSLEATIATTEH	720
Qy	721	QLTLLKTLANEKEYRHLEDEDIATVPDLQVAPPLTGKVKPLSYSKIDTTPLVQEMVKETKQL	780
Db	721	QLTLLKTLANEKEYRHLEDEDIATVPDLQVAPPLTGKVKPLSYSKIDTTPLVQEMVKETKQL	780
Qy	781	LEASARLAAENTSLVAEALVGQTSEMVASNAIVSKITSSITQPSSKTSYSGSGSSTTSNLI	840
Db	781	LEASARLAAENTSLVAEALVGQTSEMVASNAIVSKITSSITQPSSKTSYSGSGSSTTSNLI	840
Qy	841	SDVDESTQRALKAGVVMMLAAVGLTGFRFRKESK 873	
Db	841	SDVDESTQRALKAGVVMMLAAVGLTGFRFRKESK 873	

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ID      Q9A180_STRP1                Unreviewed;      1647 AA.
AC      Q9A180;
DT      01-JUN-2001, integrated into UniProtKB/TrEMBL.
DT      01-JUN-2001, sequence version 1.
DT      16-DEC-2008, entry version 51.
DE      SubName: Full=Putative cell envelope proteinase;
DR      GenomeReviews; AE004092_GR; SPY_0416.
DR      KEGG; spy:SPY_0416; -.
DR      HOGENOM; Q9A180; -.
DR      BioCyc; SPY0160490:SPY0416-MON; -.
DR      GO; GO:0009986; C:cell surface; IEA:InterPro.
DR      GO; GO:0005618; C:cell wall; IEA:InterPro.
DR      GO; GO:0005576; C:extracellular region; IEA:UniProtKB-KW.
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DR GO; GO:0016020; C:membrane; IEA:InterPro.
 DR GO; GO:0019031; C:viral envelope; IEA:UniProtKB-KW.
 DR GO; GO:0004289; F:subtilase activity; IEA:InterPro.
 DR GO; GO:0006508; P:proteolysis; IEA:InterPro.
 DR InterPro; IPR005877; Gpos_YSIRK.
 DR InterPro; IPR001899; Gram_pos_anchor.
 DR InterPro; IPR003137; PA.
 DR InterPro; IPR000209; Pept_S8_S53.
 DR InterPro; IPR015500; Peptidase_S8_subtilisin-rel.
 DR InterPro; IPR010435; Peptidase_S8A_DUF1034.
 DR Gene3D; G3DSA:3.40.50.200; Pept_S8_S53; 1.
 DR PANTHER; PTHR10795; SubtilSerProt; 1.
 DR Pfam; PF06280; DUF1034; 1.
 DR Pfam; PF00746; Gram_pos_anchor; 1.
 DR Pfam; PF02225; PA; 1.
 DR Pfam; PF00082; Peptidase_S8; 1.
 DR Pfam; PF04650; YSIRK_signal; 1.
 DR PRINTS; PR00723; SUBTILISIN.
 DR TIGRFAMs; TIGR01167; LPXTG_anchor; 1.
 DR TIGRFAMs; TIGR01168; YSIRK_signal; 1.
 DR PROSITE; PS50847; GRAM_POS_ANCHORING; 1.
 DR PROSITE; PS00136; SUBTILASE_ASP; 1.
 DR PROSITE; PS00137; SUBTILASE_HIS; 1.
 DR PROSITE; PS00138; SUBTILASE_SER; 1.
 PE 3: Inferred from homology;
 KW Complete proteome; Envelope protein; Secreted.
 SQ SEQUENCE 1647 AA; 181288 MW; F36E6CB965C291A2 CRC64;

Query Match 100.0%; Score 8503; DB 2; Length 1647;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 1647; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MEKKQRFSLRKYKSGTFSVLIGSVFLVMTTVADELSTMSEPTITNHAQQQAHLTNTE	60
Db	1	MEKKQRFSLRKYKSGTFSVLIGSVFLVMTTVADELSTMSEPTITNHAQQQAHLTNTE	60
Qy	61	LSSAESKSDTSQITLKTNREKEQSQDLVSEPTTTELADTAASMAN TGSDATQKSASLP	120
Db	61	LSSAESKSDTSQITLKTNREKEQSQDLVSEPTTTELADTAASMAN TGSDATQKSASLP	120
Qy	121	PVNTDVHDVVKTKGAWDKGYKGQKVVAVIDTGIDPAHQSMRISDVSTAKVKS KEDMLAR	180
Db	121	PVNTDVHDVVKTKGAWDKGYKGQKVVAVIDTGIDPAHQSMRISDVSTAKVKS KEDMLAR	180
Qy	181	QKAAGINYSWINDKVVF AHNYVENS DNIKENQFEDFEDWENFEFDAEAE PKAIKKHKI	240
Db	181	QKAAGINYSWINDKVVF AHNYVENS DNIKENQFEDFEDWENFEFDAEAE PKAIKKHKI	240
Qy	241	YRPQSTQAPKETVIKTEETD GSHDIDWTQTDDDTKYESHGMHVTGIVAGNSKEAAATGER	300
Db	241	YRPQSTQAPKETVIKTEETD GSHDIDWTQTDDDTKYESHGMHVTGIVAGNSKEAAATGER	300
Qy	301	FLGIAPEAQVMFMRV FANDIMGSAESLFIKAIEDAVALGADV INLSLGTANGAQLSGSKP	360
Db	301	FLGIAPEAQVMFMRV FANDIMGSAESLFIKAIEDAVALGADV INLSLGTANGAQLSGSKP	360
Qy	361	LMEAIEKAKKAGSVVVAAGNERVYGS DHD DPLATNP DYGLVGS PSTGRTP TSVA AINSK	420
Db	361	LMEAIEKAKKAGSVVVAAGNERVYGS DHD DPLATNP DYGLVGS PSTGRTP TSVA AINSK	420
Qy	421	WVIQRLMTVKEL ENRADLNHGKAIYSESVD FDKIDKSLGYDKSHQFAYVKES TDAGYNAQ	480
Db	421	WVIQRLMTVKEL ENRADLNHGKAIYSESVD FDKIDKSLGYDKSHQFAYVKES TDAGYNAQ	480
Qy	481	DVKGKIALIERDPNKTYDEMIALAKKHGALGV LIFNNKPGQSNRSMRLTANGMGIPSAFI	540
Db	481	DVKGKIALIERDPNKTYDEMIALAKKHGALGV LIFNNKPGQSNRSMRLTANGMGIPSAFI	540

Qy	541	SHEFGKAMSQNLNGNGTGSLEFDSVSVKAPSQKGNEMNHFSNWLTS	SDGYLKPDITAPGGD	600
Db	541	SHEFGKAMSQNLNGNGTGSLEFDSVSVKAPSQKGNEMNHFSNWLTS	SDGYLKPDITAPGGD	600
Qy	601	IYSTYNDNHYGSQTGTSMAS PQIAGASLLVKQYLEKTQPNLPKEKIADIVKNLLMSNAQI		660
Db	601	IYSTYNDNHYGSQTGTSMAS PQIAGASLLVKQYLEKTQPNLPKEKIADIVKNLLMSNAQI		660
Qy	661	HVNPETKTTTSPRQQGAGLLNIDGAVTSGLYVTGKDNYSISLGNITDTMTFDVTVHNLS		720
Db	661	HVNPETKTTTSPRQQGAGLLNIDGAVTSGLYVTGKDNYSISLGNITDTMTFDVTVHNLS		720
Qy	721	NKDCTLRYDTELLTDHVD P QKGRFTLTSHSLKTYQGGEVTVPANGKVTVRVTMDVSQFTK		780
Db	721	NKDCTLRYDTELLTDHVD P QKGRFTLTSHSLKTYQGGEVTVPANGKVTVRVTMDVSQFTK		780
Qy	781	ELTKQMPNGYYLEGFVFRDSDQDQLNRVNIPFVGFKQGFENLAVAEEESIYRLKSQGGKTG		840
Db	781	ELTKQMPNGYYLEGFVFRDSDQDQLNRVNIPFVGFKQGFENLAVAEEESIYRLKSQGGKTG		840
Qy	841	FYFDESGPKDDIYVGKHTGLVTLGSETNVSTKTI	SDNGLHTLGT FKNADGKFILEKNAQ	900
Db	841	FYFDESGPKDDIYVGKHTGLVTLGSETNVSTKTI	SDNGLHTLGT FKNADGKFILEKNAQ	900
Qy	901	GNPVLAI SPNGDNNQDFAAFKGVFLRKYQGLKASVYHASDKEHKNPLWVSPESFKGDKNF		960
Db	901	GNPVLAI SPNGDNNQDFAAFKGVFLRKYQGLKASVYHASDKEHKNPLWVSPESFKGDKNF		960
Qy	961	NSDIRFAKSTTLTGTA FSGKSLTGAELPDGHYHYVVSYPDVVGAKRQEMTFDMILDRQK		1020
Db	961	NSDIRFAKSTTLTGTA FSGKSLTGAELPDGHYHYVVSYPDVVGAKRQEMTFDMILDRQK		1020
Qy	1021	PVLSQATFDPETNRFKPEPLKDRGLAGVRKDSVFYLERKDNKPYTVTINDSYKYVSVEDN		1080
Db	1021	PVLSQATFDPETNRFKPEPLKDRGLAGVRKDSVFYLERKDNKPYTVTINDSYKYVSVEDN		1080
Qy	1081	KTFVERQADGSFILPLDKAKLGDFFYMVEDFAGNVAIAKLGDHLPQTLGKTPIKLLTDG		1140
Db	1081	KTFVERQADGSFILPLDKAKLGDFFYMVEDFAGNVAIAKLGDHLPQTLGKTPIKLLTDG		1140
Qy	1141	NYQTKETLKDNL EMTQSDTGLVTNQAQLAVVHRNQPQSQLTKMNQDFFISPNEDGNKDFV		1200
Db	1141	NYQTKETLKDNL EMTQSDTGLVTNQAQLAVVHRNQPQSQLTKMNQDFFISPNEDGNKDFV		1200
Qy	1201	AFKGLKNNVYNDLTVNVYAKDDHQQTPIWSSQAGASVSAIESTAWYGITARGSKVMPGD		1260
Db	1201	AFKGLKNNVYNDLTVNVYAKDDHQQTPIWSSQAGASVSAIESTAWYGITARGSKVMPGD		1260
Qy	1261	YQYVVVYRDEHGKEHQKYTISVNDKKPMITQGRFDTINGVDHFTPDKTKALDSSGIVRE		1320
Db	1261	YQYVVVYRDEHGKEHQKYTISVNDKKPMITQGRFDTINGVDHFTPDKTKALDSSGIVRE		1320
Qy	1321	EVFYLA KNGRKFVDVTEGKG DITVSDNKVYIPKNPDGSYTI SKRDGVTLS DYYYLVEDRA		1380
Db	1321	EVFYLA KNGRKFVDVTEGKG DITVSDNKVYIPKNPDGSYTI SKRDGVTLS DYYYLVEDRA		1380
Qy	1381	GNVSFATLRDLKAVGKDKAVVNFGLDLPVPEDKQIVNFTYLV RDADGKPIENLEYNNSG		1440
Db	1381	GNVSFATLRDLKAVGKDKAVVNFGLDLPVPEDKQIVNFTYLV RDADGKPIENLEYNNSG		1440
Qy	1441	NSLILPYGKYTV ELLTYDTNAAKLES D KIVSF T L S A D N N F Q Q V T F K I T M L A T S Q I T A H F D		1500
Db	1441	NSLILPYGKYTV ELLTYDTNAAKLES D KIVSF T L S A D N N F Q Q V T F K I T M L A T S Q I T A H F D		1500
Qy	1501	HLLPEGSRVSLKTAQDQLIPLEQSLYVPKAYGKTVQEGTYEVVVSLPKGYRIEGNTKVNT		1560
Db	1501	HLLPEGSRVSLKTAQDQLIPLEQSLYVPKAYGKTVQEGTYEVVVSLPKGYRIEGNTKVNT		1560

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Qy      1561 LPNEVHELRLVVKVGDAASDSTGDHKVMSKNNSQALTASATPTKSTTSATAKALPSTGEK 1620
          |||
Db      1561 LPNEVHELRLVVKVGDAASDSTGDHKVMSKNNSQALTASATPTKSTTSATAKALPSTGEK 1620
          |||
Qy      1621 MGLKLRIVGLVLLGLTCVFSRKKSTKD 1647
          |||
Db      1621 MGLKLRIVGLVLLGLTCVFSRKKSTKD 1647

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One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to make immunogenic compositions that include combination of GAS antigens in view of the teachings of Dale and Ferretti et al because Dale teach multivalent vaccines when administered to huams evoke bactericidal antibodies without toxic reactions and Ferretti et al taught GAS virulent antigens (13 antigens) including SEQ.ID.NO:1 and Spy416. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to make composition comprising various combination of antigens to treat or prevent Streptococci as suggested by Dale and Ferretti et al.

17. Claims 1 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dale 1999 New vaccines and new vaccine technology, 13:227-243 in view of Ferretti et al PNAS 2001, 98:4658-4663.

Claim 23 is drawn to a kit comprising an immunogenic composition comprising a combination of *Streptococcus pyogenes* (GAS) antigens, said combination consisting of two to ten GAS antigens, wherein said combination includes a Spy0269 antigen.

Immunogenic composition have been discussed and rejected above in Biswas et al or Telford J et al. However, the prior art does not teach a kit comprising said immunogenic composition.

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed in the form of a kit with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention and furthermore the claim would have been obvious because the kit is well known in the art and within the capabilities of one skilled in the art. Also of important note is the fact that a person of ordinary skill in the art has good reason to pursue the known option of keeping the antigens in a kit format for the convenience and economy of the user which is within his or her technical grasp and therefore it is not the product of innovation but of ordinary skill and common sense.

Remarks

18. No claims are allowed.

The IDS filed on 1/19/06 is reviewed and a signed copy of the same is attached to this action.

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Conclusion

19. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor and Robert B. Mondesi on 571)272-0956.

Respectfully,
/Padma V Baskar/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645